



hVEGF-A (VASCULAR ENDOTHELIAL GROWTH FACTOR-A, HUMAN)

The Singulex plasma VEGF assay provides the power needed to use VEGF as a biomarker for disease and the sensitivity to quantify VEGF in healthy human subjects as well as those undergoing anti-VEGF therapy.

BIOLOGY AND DISEASES

VEGF-A, commonly known as VEGF, is one member of a family of secreted glycoproteins that promote endothelial cell growth, survival, migration, and vascular permeability, all of which contribute to angiogenesis. The binding of VEGF to its receptor triggers the activation of a cell signaling pathway that is critical for the growth of blood vessels from preexisting vasculature. VEGF is implicated in a variety of diseases, including several cancers, age-related macular degeneration, diabetic retinopathy and rheumatoid arthritis. As such, it is an attractive candidate for the development of therapies for these diseases, particularly cancer.

THERAPIES

The first anti-VEGF drug, the monoclonal antibody Avastin, was approved by the FDA in 2004 and is approved to treat metastatic colon and non small-cell lung cancer. The drug is also under study for the treatment of many other cancers. Other compounds that target VEGF-mediated cell signaling include the monoclonal antibody fragment Lucentis, approved to treat age-related macular degeneration, and two small molecules, Sutent and Nexavar, which target receptor tyrosine kinases, including the VEGF receptor. Other drug candidates targeting this path are in development.

UNMET NEED

With the efficacy seen with drugs that target VEGF and its pathway, VEGF will remain an attractive development target. In addition, as researchers study various cancers and other diseases where VEGF signaling is implicated, measuring small changes in VEGF levels will help them understand biological changes that occur as disease progresses. However, current commercially available immunoassays can only measure elevated concentrations of VEGF. They are not sensitive enough to measure VEGF in plasma obtained from healthy human subjects or detect the small changes in VEGF levels that may indicate an early disease state.

SINGULEX ANSWER

The Singulex hVEGF assay increases the clinical utility of hVEGF by allowing scientists to detect very low levels of hVEGF and measure small changes in its level that can provide insights into drug efficacy or disease progression. The hVEGF assay can quantify as little as 0.15 pg of free hVEGF per mL of plasma (<20% CV). This enables the accurate detection of hVEGF in plasma with ranges from 0.04–2000 pg/mL.

This assay will allow investigators to:

1. Measure the efficacy and dosing of therapeutics designed to lower the levels of VEGF, particularly when VEGF levels should go much lower than that seen in normal states.
2. Design more robust clinical and preclinical studies when VEGF concentration is used as a therapeutic endpoint.
3. Understand how VEGF levels change in patients as they transition from healthy to diseased states with cancer and other diseases involving angiogenesis.

ERENNA TECHNOLOGY ACCESS PROGRAM.

Through the Erenna Technology Access Program (ETAP), Singulex offers an interactive, results-driven solution to biomarker challenges faced by the pharmaceutical industry during product development. Singulex assists the development programs of our ETAP collaborators by developing customer-driven assays and access to a menu of fully-validated assays. Participants in ETAP gain access to the Singulex Erenna Immunoassay System, our proven expertise developing high-value immunoassays and our world-class customer support. Together with Singulex, our ETAP collaborators are expanding the utility of protein biomarkers and using them as tools to measure disease progression, drug efficacy and toxicity.

TABLE 1: Analytical sensitivity of the Singulex hVEGF-A assay.

Lower Limit of Detection (LoD)	0.04 pg/mL
Lower Limit of Quantification (LLoQ)	0.15 pg/mL
Reading Range	0.04–2000 pg/mL

Erenna® System



TABLE 2: hVEGF-A assay low-end standard curve data.

[hVEGF-A] pg/mL	Detected Events	Std Dev	CV
21.0	5781	82	1%
6.9	2541	132	5%
2.3	1080	40	4%
0.8	471	44	9%
0.3	251	26	10%
0.1	172	10	6%
0	152	10	6%

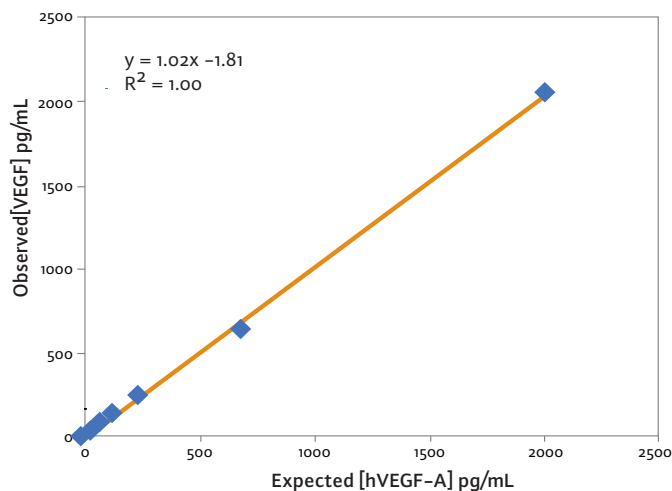
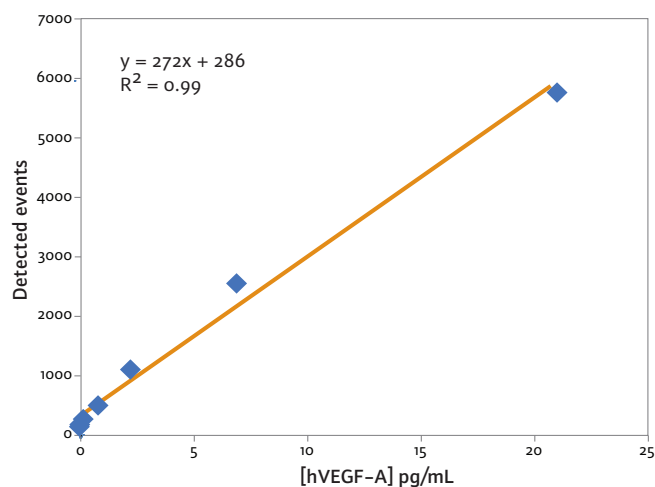
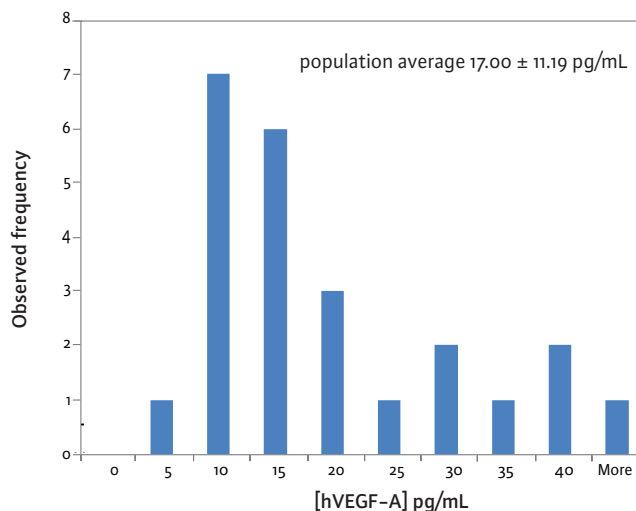


FIGURE 1: hVEGF-A assay low-end standard curve signal.

FIGURE 2: hVEGF-A assay curve fit.

These standard curves are for representational purposes only. A standard curve must be run with each assay.

Copyright © 2009, Singulex Inc. Singulex and Erenna are trademarks of Singulex, Inc.